

**IN VIVO GENE SILENCING BY  
CHEMICALLY MODIFIED AND STABLE siRNA**

**Abstract of the Disclosure**

5 The present invention provides compositions for RNA interference and methods of use thereof. In particular, the invention provides small interfering RNAs (siRNAs) having modification that enhance the stability of the siRNA without a concomitant loss in the ability of the siRNA to participate in RNA interference (RNAi). The invention also provides siRNAs having modification that increase targeting efficiency.

10 Modifications include chemical crosslinking between the two complementary strands of an siRNA and chemical modification of a 3' terminus of a strand of an siRNA. Preferred modifications are internal modifications, for example, sugar modification, nucleobase modification and/or backbone modifications. Such modifications are also useful, *e.g.*, to improve uptake of the siRNA by a cell. Functional and genomic and

15 proteomic methods are featured. Therapeutic methods are also featured.